Remarks

Prior to this Amendment, claims 1-22, 24, and 27 were pending. By this Amendment, claims 2, 13-22, 24, and 27 have been canceled without prejudice to the Applicants' right to prosecute these claims in continuing applications. New claims 29-56 have been added. Therefore, following entry of this Amendment, claims 1, 3-12, and 29-56 will be pending.

Claims 1, 3-8, and 10-12 have been amended herein. Support for these amendments is found in the specification as follows:

Claim 1 has been amended to recite that the adjuvant does not include saponin. Support for this recitation is found in the specification at page 8, lines 7-26, especially line 21. Claim 1 has been amended to recite that the clinical disease includes respiratory pneumonia. Support for this recitation is found in the specification at Example 7, page 21, line 27 to page 22, line 22 and the abstract.

Claim 3 has been amended to clarify that the *Mycoplasma bovis* biotype is inactivated. Support for this amendment is found in the specification at page 4, lines 6-19.

Claim 4 has been amended to clarify that the *Mycoplasma bovis* biotype is attenuated. Support for this amendment is found in the specification at page 4, lines 21-29.

Claim 5 has been amended to recite that the vaccine includes an adjuvant that does not contain saponin. Support for this recitation is found in the specification at page 8, lines 7-26, especially line 21.

Claim 6 has been amended to clarify that the *Mycoplasma bovis* biotype is inactivated. Support for this amendment is found in the specification at page 4, lines 6-19.

Claim 7 has been amended to clarify that the *Mycoplasma bovis* biotype is attenuated. Support for this amendment is found in the specification at page 4, lines 21-29.

Claim 8 has been amended to place it into independent form.

Claim 10 has been amended to clarify that the *Mycoplasma bovis* biotype is inactivated. Support for this amendment is found in the specification at page 4, lines 6-19.

Claim 11 has been amended to clarify that the *Mycoplasma bovis* biotype is attenuated.

Support for this amendment is found in the specification at page 4, lines 21-29.

Claim 12 has been amended merely to correct its grammar.

Support for new claims 29-56 is found in the application as follows:

Support for new claim 29 is found in the specification at page 18, line 24 to page 20, line 17; at page 20, line 20 to page 21, line 25 (see in particular page 21, lines 11-15); at page 22, line 24 to page 23, line 3 (see in particular page 22, lines 29-31); at page 23, lines 5-15 (see in particular page 23, lines 13-14).

Support for new claim 30 is found in the specification at page 9, line 6.

Support for new claim 31 is found in the specification at page 5, lines 23-25 and page 9, lines 1-2.

Support for new claim 32 is found in the specification at page 5, lines 22-23.

Support for new claim 33 is found in the specification at page 10, line 5 and page 10, line 8.

Support for new claim 34 is found in the specification at page 5, lines 12-13, Figures 1 and 2.

Support for new claim 35 is found in the specification at page 12, lines 6-28; Figures 1 and 2; and page 5, line 13.

Support for new claim 36 is found in the specification at page 12, line 4 to page 14, line 13.

Support for new claim 37 is found in the specification at page 12, line 10.

Support for new claim 38 is found in the specification at page 12, lines 13-14.

Support for new claim 39 is found in the specification at page 12, lines 15-28; and Figures 1 and 2.

Support for new claim 40 is found in the specification at page 18, line 24 to page 19, line 31.

Support for new claim 41 is found in the specification at page 23, lines 1-2.

Support for new claim 42 is found in the specification at page 8, lines 7-8.

Support for new claim 43 is found in the specification at page 8, lines 16-26 and page 11, lines 3-4. A water-oil-water emulsion is disclosed at Example 2, part D ("Adjuvanting

and Formulation of Vaccine"), page 17, lines 17-19, where in step 7 it is disclosed that an oil adjuvant is added to the inactivated *M. bovis* so as to produce a vaccine with 4% to 12% oil. One skilled in the art would understand that such a low amount of oil in the vaccine would not be enough to completely surround the aqueous phase of the vaccine and thus one skilled in the art would understand this passage to be a disclosure of an water-oil-water emulsion.

Support for new claim 44 is found in the specification at page 4, lines 13-17.

Support for new claim 45 is found in the specification at page 4, lines 17-19 and page 16, lines 22-28.

Support for new claim 46 is found in the specification at page 5, lines 12-13, Figures 1 and 2.

Support for new claim 47 is found in the specification at page 12, lines 6-28; Figures 1 and 2; and page 5, line 13.

Support for new claim 48 is found in the specification at page 12, line 4 to page 14, line 13.

Support for new claim 49 is found in the specification at page 12, line 10.

Support for new claim 50 is found in the specification at page 12, lines 13-14.

Support for new claim 51 is found in the specification at page 12, lines 15-28; and Figures 1 and 2.

Support for new claim 52 with respect to the recitation of adjuvants is found in the specification at page 8, lines 16-26 and page 11, lines 3-4. A water-oil-water emulsion is disclosed at Example 2, part D ("Adjuvanting and Formulation of Vaccine"), page 17, lines 17-19, where in step 7 it is disclosed that an oil adjuvant is added to the inactivated *M. bovis* so as to produce a vaccine with 4% to 12% oil. One skilled in the art would understand that such a low amount of oil in the vaccine would not be enough to completely surround the aqueous phase of the vaccine and thus one skilled in the art would understand this passage to be a disclosure of an water-oil-water emulsion. Support for new claim 51 with respect to the recitation of a "whole-cell" vaccine is found in the specification at page 16, lines 22-28. While the phrase "whole-cell" does not appear in this portion of the specification, it would be clear to one skilled in the art that the vaccine described in this portion of the specification is a

whole-cell vaccine. This is because the process of preparing a vaccine described in this portion begins with whole *Mycoplasma bovis* cells in culture (see page 16, line 23) and there are no steps described in which components of the whole cells are fractionated, and at the end of the process "cells" are concentrated for use as a vaccine (see page 16, lines 27-28). Further support is found at page 9, lines 27-28, which makes clear that the vaccine can comprise either whole-cells of *Mycoplasma bovis* ("inactivated or attenuated M. bovis biotypes") or non-whole-cell portions of *Mycoplasma bovis* ("or a portion thereof").

Support for new claim 53 is found in the specification at page 4, lines 6-19.

Support for new claim 54 is found in the specification at page 4, lines 6-19.

Support for new claim 55 is found in the specification at page 4, lines 6-19.

Support for new claim 56 is found in the specification at at Example 7, page 21, line 27 to page 22, line 22 and the abstract.

Claim objections

Claims 8 and 22 were objected to as being substantial duplicates of one another.

The Applicants respectfully disagree but, in the interests of expediting prosecution, claim 22 has been canceled. Thus, it is submitted that this objection is now moot.

Claim 21 was objected to for failing to further limit the subject matter of claim 1, from which claim 21 depends.

The Applicants respectfully disagree but, in the interests of expediting prosecution, claim 21 has been canceled. Thus, it is submitted that this objection is now moot.

The rejections under 35 U.S.C. §112

Claims 1-12, 21-22, 24, and 27 were rejected for lack of written description due to the recitation of "wherein the vaccine does not include saponin."

The Examiner stated that this recitation contained new matter since it required that the vaccine as a whole not include saponin rather than that the adjuvant not include saponin. See the Office Action, at page 4, lines 3-8:

It should be noted that saponin can be used as an adjuvant or it can be used as a detergent. The concepts are different. Therefore, a composition that does not contain saponin is different from a composition that does not comprise saponin as an adjuvant. The "new genus" in which the vaccine per se, rather than adjuvant component as saponin is the excluded material is not supported by the original disclosure.

Claim 1 has been amended to recite that the adjuvant does not include saponin. Claim 2 has been canceled. Claims 3 and 4 depend from claim 1. Claim 5 has been amended so that it no longer recites saponin. Claims 6 and 7 depend from claim 5. Claim 8 has been amended to place it into independent form and in this form no longer recites saponin. Claims 9-12 depend from claim 8. Claims 21, 22, 24, and 27 have been canceled. Thus, the only claims that recite that any component of the vaccine does not include saponin are claims 1, 3, and 4, and those claims now recite that the adjuvant does not include saponin. Therefore, the Applicants respectfully request that this rejection be withdrawn.

Claims 8-12, 21-22, and 24 were rejected as being indefinite.

Claim 8 was rejected because "it is not clear as to whether there are one or two pharmaceutically acceptable excipients included in the vaccine composition." Claim 8 has been amended so as to obviate this rejection by making it clear that there is only one pharmaceutically acceptable excipient required. Therefore, the Applicants respectfully request that this rejection be withdrawn.

Claims 1-12, 21-22, 24, and 27 were rejected as being indefinite. The Examiner stated that it is not clear what is being referred to by the word "biotypes."

The Applicants respectfully traverse this rejection. The specification provides an explicit definition of "biotype" as being a variant that can be distinguished by one or more characteristics. In addition, the specification provides examples of the kinds of characteristics that can be used to distinguish biotypes and provides citations to literature

that provide teachings with regard to techniques that can be used to distinguish biotypes See page 5, lines 11-18:

> The term "biotype" means a variant of a species, i.e. a strain, that can be distinguished by one or more characteristics, such as ribosomal RNA sequence variation, DNA polymorphisms, serological typing, or toxin production (*see e.g.*, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989; *DNA cloning: A Practical Approach*, Volumes I and II, Glover, D.M. ed., IRL Press Limited, Oxford, 1985; Harlow and Lane, *Antibodies, A Laboratory Manual*, Cold Spring Harbor Publications, N.Y. (1988)).

The specification also provides working examples of how three different biotypes can be distinguished. See Figures 1 and 2 and the accompanying descriptive text at pages 3 and 12-14 , wherein biotypes A, B, and C are described.

It is well settled that the definiteness of a claim is not to be judged in a vacuum. Instead the claim must be viewed in the context of the disclosure of the application from which it is derived. The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1 USPQ2d 1081 (Fed. Cir. 1986). See also BJ Services Co. v. Halliburton Energy Services, Inc., 338 F.3d 1368, 1372, 67 USPQ2d 1692, (Fed. Cir. 2003): "The question becomes whether one of ordinary skill in the art would understand what is claimed when the claim is read in light of the specification."

Given the explicit teachings of the specification referred to above with respect to the meaning of biotypes, the Applicants submit that this word would be clearly understood by one skilled in the art, upon reading the specification.

The rejections under 35 U.S.C. §102(b)

Claims 1, 3, 5-6, 21, 24, and 27 were rejected as being anticipated by Boothby, *Immunologic Responses to Mycoplasma bovis*, University Microfilm International (Dissertation) 1-172, 1982 (Boothby). The Examiner stated that the Applicants must show "that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine" (Office Action, page 7, 3rd paragraph).

The Applicants respectfully traverse this rejection. There is a clear functional difference between the Applicants' vaccine and Boothby's. This indicates that Boothby's vaccine and the Applicants' vaccine are not the same.

The vaccine of the present invention does not cause unfavorable or adverse reactions. See the specification, at page 23, lines 2-3: "No unfavorable reactions resulting from the vaccine's use have been reported;" page 23, lines 14-15: "No unfavorable reactions in animals receiving the product have been reported;" page 20, line 1: "No injection reactions were observed;" and the abstract: "These vaccines demonstrate no undesirable side effects ..."

In contrast, Boothby's vaccine produces a very unfavorable reaction - all of Boothby's animals showed hypersensitivity (see Boothby, page 136, 3rd paragraph). This is a real functional difference between the Applicants' vaccine and Boothby's that must be due to the nature of the vaccine, and cannot be attributed to any "intended use" of the vaccine.

Case law holds that vaccines can be patentable over prior art based on functional characteristics. See Ex parte Plotkin, 174 USPQ 39 (Pat. Off. Bd. App. 1971). In Plotkin, the claimed vaccine had the functional characteristic of being able to be administered intranasally with high effectiveness. This was found to confer patentability to claims to the vaccine itself over the prior art.

Moreover claim 5 and dependent claim 6 therefrom require that the vaccine comprises particular biotypes that are not disclosed in Boothby. Claims 21, 24, and 27 have been canceled.

In view of the above, it is respectfully requested that this rejection be withdrawn.

The Applicants submit that the new claims are not anticipated by Boothby for the same reasons as discussed above with respect to claims 1, 3, 5-6, 21, 24, and 27 as well as for the additional reasons that are discussed below.

New independent claim 29 recites that the vaccine "is protective against *Mycoplasma bovis* mastitis in a bovine species." This recitation makes clear that the functional characteristic of being protective against mastitis is not simply an intended use but rather is a characteristic of the vaccine itself. This characteristic distinguishes over the prior art, such as the vaccine disclosed in Boothby. Given that the vaccine in Boothby clearly differs from the Applicants' vaccine (as shown by differences with respect to causing unfavorable reactions), it cannot be assumed that Boothby's vaccine is protective against mastitis.

Furthermore, publications later than Boothby indicate that Boothby could not have disclosed a vaccine protective against mastitis. For example, Heller et al., 1993, Vet. Microbiol. 37:127-133[1] did not mention that one should vaccinate to control mastitis but instead stated that culling is necessary. See page 127: "To control the spread of this disease, an early detection of the pathogen is crucial since the removal and culling of infected cows is necessary to prevent fresh infections." In Hanson, (September, 2001) Bovine Veterinarian 4-8[2] and Hanson, (October, 2001) Bovine Veterinarian 12-20[3],

[1] Reference A32 of the Information Disclosure Statement filed April 16, 2002.

[2] Reference A30 of the Information Disclosure Statement filed April 16, 2002.

[3] Reference A31 of the Information Disclosure Statement filed April 16, 2002.

methods to prevent mastitis or mitigate its effects are described but the methods do not include vaccination, indicating that no effective vaccine was known to the art.

New claims 30-33 and 40-51 depend from new claim 29 and thus the same considerations apply to these dependent claims.

New claims 34-39 depend from claim 8, which recites "at least two inactivated or attenuated *Mycoplasma bovis* biotypes." Since Boothby does not disclose a vaccine comprising more than a single biotype, Boothby does not anticipate these new claims.

New independent claim 52 recites that the vaccine comprises an adjuvant that differs from the adjuvants listed in Boothby.[4] Therefore, Boothby does not anticipate new claim 52. New claim 55 depends from new claim 52 and therefore Boothby does not anticipate new claim 55 either.

In view of the above, it is respectfully requested that this rejection be withdrawn.

Claims 1, 4, 5, and 7 were rejected as being anticipated by Thorns et al., 1980, Res. Vet. Sci. 29:328-332 (Thorns).

The Applicants respectfully traverse this rejection. All of the rejected claims are directed to vaccines that are protective against diseases caused by *Mycoplasma bovis* in bovines. Thorns does not disclose a vaccine. Thorns discloses attenuated strains of *Mycoplasma bovis* that were injected into mice. There is no disclosure in Thorns that the attenuated strains were protective against any disease in the injected mice. Thorns does not

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[4] At page 131, Boothby discloses the use of the following adjuvants:
Freund's incomplete adjuvant
N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP)
Amphotericin B
Combined magnesium/aluminum hydroxide
Killed *Bordatella pertussis*

even disclose any data that indicate the attenuated strains caused any stimulation of the immune systems of the mice against *Mycoplasma bovis.*

On pages 7 and 8 of the Office Action, the Examiner stated that the highly passaged strains in Thorns did not cause a systemic response, inflammation, or abnormal glands. The Applicants wish to point out that these responses (or lack thereof) were due to the injected strains themselves. In other words, Thorns showed that highly passaged strains were attenuated in the sense that they did not cause those responses to the same degree as low passaged strains. This is not the same as, nor is it predictive of, a showing that these attenuated strains could function as vaccines, to protect against disease caused by later exposure to *Mycoplasma bovis*. Thorns provided no evidence on that point. In particular, Thorns provided no evidence that the mice that were given the attenuated strains were protected from disease when later challenged with *Mycoplasma bovis*. Apparently, Thorns did not even challenge the mice.

Moreover, the authors of Thorns did not consider that their strains were vaccines. The authors considered that the work they disclosed provided information and a starting point for research that might someday perhaps lead to the production of a vaccine against *Mycoplasma bovis*. See page 332, right column, 3rd paragraph:

> Whatever mechanisms the virulent strains have lost or modified, they should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease. [emphasis added]

The last phrase of this sentence makes clear that the authors of Thorns did not think that they have already provided such a vaccine.

Furthermore, Thorns is completely silent on the subject of inactivated, as opposed to attenuated, vaccines. Therefore, for this reason also, Thorns does not anticipate claims 3, 6, 10, 31-33, 44-51, and 53-55, which require an inactivated vaccine.

In view of the above, it is respectfully requested that this rejection be withdrawn.

The rejection under 35 U.S.C. §103(a)

Claims 1-12, 21-22, 24, and 27 were rejected as being obvious over Boothby in view of Poumarat et al., 1994, Vet. Microbiol. 40:305-321 (Poumarat) and Thorns.

As discussed above, Boothby does not disclose a vaccine that does not cause unfavorable reactions or a vaccine that is protective against mastitis. Neither Thorns nor Poumarat provide this subject matter that is missing in Boothby. Thorns does not disclose vaccines, and certainly not vaccines that do not cause unfavorable reactions[5] or vaccines that are protective against mastitis.[6] Poumarat also does not disclose any vaccines since Poumarat is limited to a study of the antigenic characteristics of certain strains of *Mycoplasma bovis*.

Thorns and Poumarat do not contain the subject matter that is missing from Boothby, nor suggest how to obtain such subject matter. There is no teaching in Thorns or Poumarat that would enable one skilled in the art to produce a vaccine that does not cause unfavorable reactions. Therefore, one of ordinary skill in the art could not arrive at the present invention by combining Thorns and Poumarat with Boothby. Accordingly, all of the present claims are non-obvious over Boothby, Poumarat, and Thorns, and it is respectfully requested that this rejection be withdrawn.

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[5] All of the strains in Thorns caused some kind of histopathological changes, albeit some strains only caused minor changes. See the last sentence of the abstract: "the high passage strains produced only minor histopathological changes." See also the right column in Table 1 on page 329, which shows that only the control (i.e., no *Mycoplasma bovis*) injections resulted in no histopathological changes. Thus, even if Thorns disclosed vaccines, which the Applicants dispute, Thorns would not disclose vaccines that have the same functional characteristics as the Applicants' vaccine.

[6] As discussed above, Thorns provided absolutely no evidence that the strains used protected against any disease.

With respect to claims 8-12, 31-39, and 46-51, which require two or more biotypes, the Applicants wish to point out that Poumarat contradicts the Examiner's argument and teaches away from the claimed subject matter.

Poumarat divided *Mycoplasma bovis* isolates into 13 different "genomic groups." Poumarat then looked at the antigenic variability between and among these genomic groups. Although Poumarat found much antigenic variability, this variability did not correlate with membership in any particular genomic group. In other words, the same amount of antigenic variability could be found within groups as between groups. See page 318, 2nd paragraph:

> Antigenic profiles of the *M. bovis* strains obtained by immunoblotting with J008 calf serum differed markedly one from the other, the heterogeneity being equally great among strains belonging to the same genomic group and those coming from different genomic groups. There appeared to be no relation between the genomic variability of *M. bovis* and the antigenic variability ...

Because Poumarat teaches that antigenic variability is as great within *Mycoplasma bovis* groups as across *Mycoplasma bovis* groups, Poumarat teaches that there would be no gain in antigenic variability from including more than one type of *Mycoplasma bovis* in a vaccine. That is, there would be no point in having more than one type of *Mycoplasma bovis* in a vaccine. Poumarat thus discourages one of ordinary skill in the art from including more than one biotype in a vaccine. This teaches away from the subject matter of claims 8-12, 31-39, and 46-51. Thus, these claims are non-obvious over Boothby, Thorns, and Poumarat.

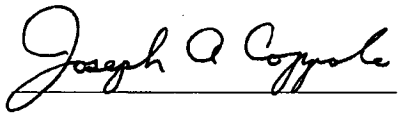
With respect to claims 29-33 and 40-51 which require that the vaccine be protective against mastitis, the Applicants wish to point out that none of Boothby, Thorns, or Poumarat discloses such a vaccine. Nor does any combination of those references suggest how to obtain such a vaccine. Thus, these claims are non-obvious over Boothby, Thorns, and Poumarat.

The time for responding to the Office Action was set for December 30, 2003. Enclosed herewith is a Petition for the Extension of Time under 37 C.F.R. § 1.136(a) for a period sufficient to permit the filing of this response and charge any corresponding fees to Kenyon & Kenyon's Deposit Account No. 11-0600.

The Applicants hereby make a Conditional Petition for any relief available to correct any defect seen in connection with this filing, or any defect seen to be remaining in this application after this filing. The Commissioner is authorized to charge Kenyon & Kenyon's Deposit Account No. 11-0600 for the Petition fee and any other fees required to effect this Conditional Petition.

Respectfully submitted,

Dated: MARCH 29, 2004



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